REMARKS

The Office Action mailed January 24, 2003, set a three-month shortened statutory period for response expiring April 24, 2003. The period for response is extended three months to expire July 24, 2003, in accordance with the Petition for Extension of Time under 37 C.F.R 1.136(a) submitted herewith. This amendment is therefore timely filed.

Claims 1-14, 16, 19-23, and 26-75 are in the application.

Claim 1 has been amended to recite an immediate release entity and a delayed release entity that contains a cationic or zwitterionic surfactant and an organic acid, and is coated with an ammonio methacrylate copolymer. Claims 9-13, 19, 20, and 58 have been amended to depend from Claim 1 and Claim 8, the limitations of which have been incorporated in Claim 1, has been cancelled.

Claims 1-4, 6, 8, 9, 27, and 28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dandiker et al, U.S. 5,425,950, on the grounds that Dandiker teaches a controlled release composition comprising a layered-tablet suitable for pulsed release of active ingredient, including hypnotic drugs, which layered-tablet comprises a rapidly disintegrating outer active layer and inner layer/layers of active ingredient that will gradually be removed after the rapidly disintegrating outer active layer is removed; that the rapidly disintegrating outer active layer dissolves within 30 minutes, and the gradually inner active layer/layers, which further comprises fillers, excipients, surfactants, lubricants, and the like, dissolves in from 1-3.5 hours; and that it would therefore have been obvious for one of ordinary skill in the art, by routine experimentation, to use a hypnotic drug in the pulsed release formulation, because Dandiker suggests that a hypnotic drug is a suitable active ingredient in his invention. The rejection is respectfully traversed and reconsideration thereof is requested.

Claim 1, as amended, is directed to a composition containing an immediate release entity and a delayed release entity wherein the latter contains a short acting hypnotic in

combination with a cationic or zwitterionic surfactant and an organic acid, and is coated with an ammonio methacrylate copolymer. As explained at page 6 of Applicants' specification the cationic or zwitterionic surfactant diffuses into the ammonio methacrylate copolymer coating and provides a change in its properties provoking a sudden rapid release. The delayed pulse is thereby accelerated and gives more complete release of the short acting hypnotic. Moreover, the organic acid provides a dissolution that is independent of pH. The Dandiker compositions require the use of a pH independent hydrophilic polymer, namely, hydroxypropyl methylcellulose. Moreover, as noted at column 10, lines 50-53, of the reference, inclusion of surfactants can give rise to higher viscosity and slower release as opposed to the accelerated and more complete release produced by the cationic or zwitterionic surfactants in Applicants' composition. Nowhere is the combination of ammonio methacrylate polymer, cationic or zwitterinoic surfactant and organic acid, or the advantages afforded thereby suggested by Dandiker. Thus, Dandiker is submitted to be incompetent to suggest the invention here claimed, and the rejection based thereon should be withdrawn.

Claims 1-4, 6, 8, 9-14, 16, 19-22, 27, 28, 31-46, and 54-67 as well as Claims 5, 7, 29, and 30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Midha et al., U.S. 6,340,476, on the basis that Midha teaches a pulsatile delivery system comprising first, second, and third dosage units having different drug release profile, which dosage units can be in the form of tablets, coated tablets, matrix tablets, matrix particles or beads, coated particles or beads, or uncoated particles or beads to be placed in a capsule and can be coated or incorporated in matrix containing polymers, such as cellulose, or methacrylate polymer/copolymer; that the drug-containing dosage unit further comprises filler, binder, disintegrant, lubricant, and surfactant, including cationic surfactant; and that the active ingredients can be selected from antidepressant drugs, analgesic, and anti-anxiety drugs, such as benzodiazepines, lorazepam, midazolam, temazepam, and triazolam. The Examiner urges

that since Midha suggests anti-anxiety drugs can be used in the pulsatile delivery system, it would have been obvious for one of ordinary skill in this art to modify Midha's delivery system using anti-anxiety drugs with the expectation of at least similar result because the reference teaches the advantageous results in the use of pulsatile delivery system to deliver anti-anxiety drugs, such as benzodiazepines, lorazepam, midazolam, temazepam, and triazolam. The Examiner further maintains that the percent release of active agent is inherent, since Midha teaches pulsatile delivery system having the same release profile, e.g., first dosage being released immediately upon administration, second dosage being released within 3-5 hours (column 12, lines 1-5). Thus, it would have been obvious for one of ordinary skill in the art, by routine experimentation, to optimize the amounts of binder, disintegrant, or coating to obtain at least similar results. For the reasons that follow, the rejection is traversed and reconsideration thereof is requested.

First of all, Midha discloses a dosage form for the pulsatile delivery of methylphenidate. The mere recitation of hundreds of other drugs that might be combined with methylphenidate, or of dozens of delayed release coatings, or of hundreds of optional excipients, does not amount to a teaching or suggestion of the particular combination of elements and ingredients in Applicants' claimed composition. Nor does the disclosure by Midha of a first dosage being released immediately and a second dosage being released within 3-5 hours suggest Applicants' invention. As disclosed at column 11, lines 56-58, of the reference, the immediate release dosage form releases the active agent within 1-2 hours following administration. Applicants' immediate release entity releases 40-70% of the total amount of the active agent in 30 minutes. Thus, contrary to the Examiner's assertion, the percent release of active agent is clearly not inherent, and nothing in Midha would have suggested the quantitative release profile of Applicants' composition. In view of the foregoing, the rejection over Midha should be withdrawn.

Claims 26 and 73-75 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Midha et al. and Cuca et al., U.S. 5,491,681. The Examiner states that although Midha does not teach that the pulsatile dosage form can be incorporated into a drinkable form, Cuca teaches that active ingredients in matrix form suitable for pulsatile release can be incorporated in a drinkable form, which active ingredients can be selected from antitussive, antihistamine, antitumor, hypnotics, and the like, and urges that it would have been obvious for one of ordinary skill in the art to modify Midha's pulsatile delivery system with the teachings of Cuca with the expectation of at least similar results.

In fact, Cuca relates to a taste-masked pharmaceutical material comprising an active ingedient, a major amount of a wax core material and a minor amount of a hydrophobic polymer. The formulation is intended to mask the noxious, bitter taste of certain drugs. The subject matter of Cuca bears no relationship in form or function to either Applicants' claimed composition or the composition of Midha. The composition of Claims 26 and 73-75 contains a constituent which upon introduction of the composition into an alcoholic or non-alcoholic beverage causes a visual change in the appearance of the drink, e.g., a change in color or a floating of the composition at the surface of the drink. As described at pages 9-11 of Applicants' specification, the purpose of such composition is to avoid administration of the hypnotic to a person in a drink without his or her knowledge. Clearly then, the Cuca reference is irrelevant to Applicants' claims; adds nothing to Midha; and neither alone nor in combination with Midha comtemplates Applicants' compositions. It is submitted that the rejection of Claims 26 and 73-75 over Midha and Cuca is without merit and should be withdrawn.

Claims 23 and 68-72 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Midha et al., in view of Bastin et al., U.S. 6,309,668, on the grounds that although Midha does not teach zolpidem as a hypnotic agent, Bastin teaches a multilayer tablet formulation

comprising hypnotic drugs, including zolpidem, and therefore, it would have been obvious for one of ordinary skill in the art to modify Midha's anti-anxiety agent (hypnotic agent) with zolpidem in view of the teachings of Bastin to obtain the claimed invention. Applicants disagree.

The Bastin reference relates to an abuse-resistant tablet containing an active substance and, in a separate layer, a gelling agent. The gelling agent prevents extraction of the active substance from the tablet to provide a solution, which would be used for illegal parenteral administration. The mere fact that Bastin discloses a tablet formulation containing zolpidem would not, either alone or in combination with Midha, suggest Applicants' timed dual release composition. Thus, Bastin adds nothing to Midha, and the rejection based thereon should be withdrawn.

Claims 47-53 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Midha et al., and Gallopo et al., U.S. 5,176,901. The Examiner maintains that although Midha does not specifically teach cocamidopropylbetaine as a cationic surfactant, Gallopo teaches a useful cationic surfactant including cocamidopropylbetaine and, therefore, it would have been obvious for one of ordinary skill in the art to modify Midha's cationic surfactant using the cocamidopropylbetaine in view of the teaching of Gallopo with the expectation of at least similar result, because the cocamidopropylbetaine is a well-known and useful cationic surfactant in the pharmaceutical art.

The rejection is submitted to be without merit. Gallopo discloses dentifrice compositions which may contain cocamidopropylbetaine. However, the mere fact that this surfactant could be used in a dentifrice composition is not tantamount to a teaching that it would be useful in the composition of Midha, let alone in Applicants' claimed composition. There is simply nothing in the combined teaching of Midha and Gallopo that would suggest the combination of an ammonio methacrylate copolymer coating and cocamidopropylbetaine

wherein the surfactant provides a change in the properties of the polymer permitting a sudden release of the polymer-coated active agent. Withdrawal of the rejection is requested.

There being no remaining issues, this application is believed to be in condition for favorable reconsideration and early allowance and such actions are earnestly solicited.

Respectfully submitted,

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